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EFFECTS OF HYPODYNAMIA ON THE HEMOCOAGULATIVE PROPERTIES
OF THE VASCULAR WALL AND MYOCARDIUM

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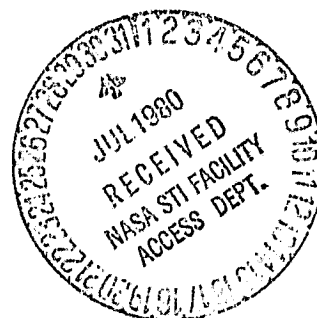
Translation of "Vliyaniye gipodinamii na gemokoaguliruyushchiye svoystva
sosudistoy stenki i miokarda," Kardiologiya,
Vol. 18, No. 3, March 1978, pp 126-129.

(NASA-TM-76199) EFFECTS OF HYPODYNAMIA ON
THE HEMOCOAGULATIVE PROPERTIES OF THE
VASCULAR WALL AND MYOCARDIUM (National
Aeronautics and Space Administration) 9 p
HC A02/MF A01

N80-27992

Unclass
28032

CSC 06C G5/51



STANDARD TITLE PAGE

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|--|--|--|--|--|--|
| 1. Report No. NASA TM-76199 | | 2. Government Accession No. | | 3. Recipient's Catalog No. | |
| 4. Title and Subtitle EFFECTS OF HYPODYNAMIA ON THE HEMOCOAGULATIVE PROPERTIES OF THE VASCULAR WALL AND MYOCARDIUM | | | | 5. Report Date June 1980 | |
| | | | | 6. Performing Organization Code | |
| 7. Author(s) V. I. Inchina | | | | 8. Performing Organization Report No. | |
| | | | | 10. Work Unit No. | |
| 9. Performing Organization Name and Address Leo Kanner Associates Redwood City, California 90463 | | | | 11. Contract or Grant No. | |
| | | | | 13. Type of Report and Period Covered Translation | |
| 12. Sponsoring Agency Name and Address National Aeronautics and Space Administration Washington, D. C. 20546 | | | | 14. Sponsoring Agency Code | |
| | | | | | |
| 15. Supplementary Notes Translation of "Vliyaniye gipodinamii na gemokoaguliruyushchiye svoystva sosudistoy stenki i miokarda," <u>Kardiologiya</u> , Vol. 18, No. 3, March 1978, pp 126-129. | | | | | |
| 16. Abstract The hemocoagulative properties of the aorta (laminar), myocardi- um, hollow veins, and fibrinolytic capacity of tissues were studied in 14 rabbits subjected to 7 days of restricted mobility and compared to those of 10 control animals. Two tables of results show that, as a result of hypodynamia, the thromboplastic activity of the inner and middle layers of the aorta together with the destruction of endothelium increases the hemocoagulative potential and creates the threat of thrombogenesis. There is also an increase in fibrin-stabilizing acti- vity for all tissues. | | | | | |
| 17. Key Words (Selected by Author(s)) | | | 18. Distribution Statement This copyrighted Soviet work is reproduced and sold by NTIS under license from VAAP, the Soviet copyright agency. No further copying is permitted without per- mission from VAAP. | | |
| 19. Security Classif. (of this report) Unclassified | | 20. Security Classif. (of this page) Unclassified | | 21. No. of Pages 8 | |
| | | | | 22. Price | |

EFFECTS OF HYPODYNAMIA ON THE HEMOCOAGULATIVE PROPERTIES
OF THE VASCULAR WALL AND MYOCARDIUM

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A number of authors are of the opinion that hypodynamia is one of the factors /126* leading to the development of atherosclerosis [3-8]. The heart and the vascular wall because of a complex of compounds capable of hemocoagulating and fibrinolytic activity are the prime movers in the regulation of the process of blood coagulation [4, 6]. A change in the thromboplastic fibrinolytic activity of the vascular walls in atherosclerosis leads to hypercoagulemia and thrombogenesis [4, 5].

The experiments were conducted on chincilla rabbits weighing 2-3 kg under restricted mobility conditions according to the method of V. V. Tyakovin [8]. There were 10 animals in the control group and 14 rabbits in the experimental group maintained in hypodynamia for 7 days. An examination was made of the hemocoagulation qualities of the aorta (laminar), of the myocardium and of the hollow veins using conventional methods [1]. The fibrinolytic quality of the tissues was assessed by the euglobulin method with modifications for the determination of the content of fibrinolytic activators and the overall fibrinolytic activity of the tissues [7].

Dissection of the experimental animals showed pronounced plethora of the parenchymatic organs: liver, kidneys and lungs. In most of the rabbits the heart was enlarged due to the dilatation of both ventricles. One noted a change in the coloring of the intima of the aorta which was a deep yellow. In the aorta one noted roughness of the inner layer and ulceration.

When mobility is restricted, the thromboplastic qualities of the inner and middle layers of the aorta are increased 5-10 times (Table I), the activity of tissue thrombokinases in the adventitia is a bit reduced but does not change in the heart muscles and hollow veins.

* Numbers in the margin indicate pagination in the foreign text.

TABLE I. THROMBOPLASTIC PROPERTIES OF THE AORTA, MYOCARDIUM AND HOLLOW VEINS

| Index | Control | Intima | Media | Adventitia | Myocardium | Veins /127 |
|---|---------------------|--|---|--|--|--|
| Recalcification time (degree of dilution) | | 1:10 000 ($< 0,05$) 1:50 000 | 1:5 000 ($< 0,05$) 1:50 000 | 1:10 000 ($< 0,01$) 1:1 000 | 1:5 000 ($< 0,01$) 1:5 000 | 1:50 000 ($< 0,02$) 1:50 000 |
| Use of prothrombin | | ($< 0,01$) 1:10 000 ($< 0,01$) 1:50 000 | ($< 0,001$) 1:5 000 ($< 0,01$) 1:10 000 | ($< 0,01$) 1:10 000 ($< 0,001$) 1:1 000 | ($< 0,001$) 1:5 000 ($< 0,01$) 1:5 000 | ($< 0,05$) 1:50 000 ($< 0,01$) 1:50 000 |
| Plasma tolerance of heparin, sec. | $\frac{430}{300}$ | ($< 0,001$) 141,2 \pm 29 ($< 0,001$) 128,2 \pm 22,9 | ($< 0,05$) 149,2 \pm 31 ($< 0,001$) 108 \pm 21 | ($< 0,01$) 125 \pm 35,3 ($< 0,001$) 95 \pm 18 | ($< 0,01$) 63,3 \pm 15,3* ($< 0,001$) 61,8 \pm 21,5 | ($< 0,01$) 69 \pm 11* ($< 0,001$) 63 \pm 21 |
| Antiheparin activity, sec. | $\frac{136,5}{139}$ | ($< 0,001$) 50 \pm 17 ($< 0,001$) 39 \pm 15,1 | ($< 0,001$) 42,4 \pm 2,8 ($< 0,001$) 50 \pm 13,3 | ($< 0,001$) 37,1 \pm 11,6 ($< 0,001$) 45,5 \pm 13 | ($< 0,001$) 31 \pm 10 ($< 0,001$) 45 \pm 15,5 | ($< 0,001$) 18 \pm 21 ($< 0,001$) 75 \pm 23 |

Note: Here and in Table II: numerator - indices of controls, denominator - indices of experimental animals; in parentheses - reliability of differences (p) calculated in relation to plasma of controls; asterisk - reliable difference for indices of intact and experimental animals.

TABLE II. EFFECT OF EXTRACTS FROM THE AORTA, MYOCARDIUM AND HOLLOW VEINS ON SOME PARAMETERS OF HEMOCOAGULATION

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| Index | Control | Intima | Media | Adventitia | Myocardium | Veins |
|--|---------------------|---|--|--|---|--|
| Ordinary plasma prothrombin time, sec. | $\frac{36,5}{34,6}$ | 31,2 \pm 1,1 ($< 0,05$) 31,6 \pm 1,4 ($< 0,05$) | 29,7 \pm 0,9 ($< 0,001$) 33 \pm 1,2 ($< 0,05$) | 30,9 \pm 0,5 ($< 0,05$) 31,5 \pm 1,2 ($< 0,001$) | 28,3 \pm 2,6 ($< 0,05$) 27 \pm 1,1 ($< 0,01$) | 26,1 \pm 1,5 ($< 0,05$) 31 \pm 1,1 ($< 0,001$) |
| Same for plasma minus factor V | $\frac{71,3}{84,1}$ | 78,7 \pm 2,7 ($< 0,02$) 87,3 \pm 8,4 ($< 0,05$) | 77,1 \pm 1,6 ($< 0,05$) 87,6 \pm 7,2 ($< 0,05$) | 73,1 \pm 2,2 ($< 0,001$) 98,6 \pm 2,7 ($< 0,001$) | 58,2 \pm 3,8 ($< 0,05$) 83,8 \pm 9,1 ($< 0,05$) | 35 \pm 7,0 ($< 0,05$) 101,2 \pm 4 ($< 0,001$) |
| Plasma thrombin time, sec. | $\frac{31,1}{32,5}$ | 35,4 \pm 1,2 ($< 0,02$) 35,4 \pm 0,8 ($< 0,001$) | 31,7 \pm 0,9 ($< 0,05$) 35,2 \pm 1,7 ($> 0,05$) | 32,9 \pm 1,2 ($< 0,01$) 31,2 \pm 1,1 ($< 0,001$) | 31,5 \pm 1,4 ($< 0,001$) 32,1 \pm 1,1 ($< 0,05$) | 35 \pm 7,0 ($< 0,001$) 31,1 \pm 0,9 ($< 0,001$) |
| Free heparin time, sec. | $\frac{6}{5,6}$ | 8 \pm 2,9 ($< 0,05$) 6,0 \pm 0,8 ($< 0,01$) | 6,2 \pm 1,6* ($< 0,01$) 6,8 \pm 1,1 ($> 0,05$) | 5,7 \pm 1,3 ($< 0,05$) 3,1 \pm 0,9 ($< 0,001$) | 4,8 \pm 1 ($< 0,001$) 1,1 \pm 1 ($> 0,05$) | 11,6 \pm 2,8 ($< 0,001$) 4 \pm 1,1 ($< 0,05$) |

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Extracts of all tissues studied, both from the control and experimental animals, increased the resistance of plasma to heparin, which is conditioned by the presence of thromboplastic and antiheparin substances (see Table I). Seven days of hypodynamia increases the ability of the tissues to neutralize heparin. Thus, while extracts of the intima of the aorta in the case of the control animals increases tolerance of plasma toward heparin 3.2 times, it does so only 2.3 times for the experimental animals. Similar changes are noted in an examination of extracts of the middle and outer layers of the aorta.

One of the reasons for the reduction of the heparin-neutralizing properties of tissues in hypodynamia is probably a reduction in the activity of the antiheparin factor in the middle layer of the aorta by 2.6 times, in the adventitia and myocardium by 3.1 times, and in the hollow veins by 1.8 times. Antiheparin properties of the intima are somewhat increased (cf. Table I).

Extraction from the intima and adventitia produces some lengthening and from the media, myocardium and hollow veins some shortening of the prothrombin time of ordinary plasma (Table II). In the course of the experiment the level of tissue prothrombokinases in the aorta went up slightly. However, as judged by that index, the activity of the extracts of the myocardium and hollow veins was somewhat weakened, this being evidently associated with an increase in the anticoagulating properties of these tissues. All the tissues studied for intact rabbits increased the transition time for the changing of fibrinogen into fibrin which is a function of the presence of anticoagulants with an antithrombin effect (see Table II). In animals subjected to immobilization the anticoagulation effect of the tissues is weakened except for the middle layer of the aorta where antithrombin activity is increased by 8.3%. In experiments with a 0.1% of protamine sulfate we found that the anticoagulation potential of the media is associated with an increase in the content not only of heparin but also of another type of anticoagulants.

The density and rate of lysis of a thrombus is largely dependent upon tissue fibrinase which promotes the transition of dissolved fibrin into the undissolved type. All tissues studied, both for the control and experimental animals, showed a fairly high capacity for stabilizing fibrin. As a result of hypodynamia that lasted 7 days there was an increase in tissue fibrinase activity by 21.2% (intima), in the media by 23.9% and the adventitia by 20%. There was no significant change in the

fibrinase activity of the myocardium.

The fibrinolytic activity of the tissues of intact and experimental rabbits was very low, which is associated with the high level of inhibitors and nearly total absence of fibrinolysis activators in the aorta. In the course of the experiment the level of fibrinolysis stimulators grows in the middle and outer layers of the aorta as well as in the myocardium, although overall fibrinolytic activity of these tissues remains low despite a reduction in the amount of fibrinolysis inhibitors. Only in the wall of the hollow veins did one notice an increase in fibrinolytic capability up to 21.2%. Meanwhile extracts of the inner layer of the aorta depressed fibrinolysis in the first series of experiments to a much greater degree than in the control. In hypodynamia the antifibrinolytic properties of the myocardium are reduced from 39.3 to 7.4%.

As has been remarked, the vascular wall is the different regulator of the process of blood coagulation. According to the data of some authors [9, 10], restricted mobility increases the coagulation activity of the blood. One of the factors that activate the hemostatic system is a change in the vascular wall. V. V. Tyavokin demonstrated changes in the intima of the aorta [8] in the case of some rabbits already during the first 24 hours of restricted mobility. The interior surface of the aorta became rough and during later periods of hypodynamia there was development of edema of the subendothelial layer which preceded the development of atherosclerotic platelets.

In our experiments the increase in thromboplastic activity of the middle and inner layers of the aorta together with the destruction of endothelium increases hemocoagulation potential and constitutes a threat of thrombogenesis. A reduction in the anticoagulant properties of the endothelial layer, an increase in its anti-heparin and fibrinase activity, and a reduction in the fibrinolytic activity of the intima makes possible the development of intravascular coagulation which is even more authentic. At the same time we note a compensatory reaction in the vascular bed. The sharp increase in the anticoagulant properties of the adventitia may possibly be associated with the degranulation of fat cells noted by some authors in restricted mobility [2]. Similar changes occur in the venous bed, preventing thrombogenesis when blood circulation slows down. At the same time there is a reinforcement of the fibrinolytic capacity of the venous bed.

Conclusions

1. The myocardium, all layers of the aorta and the hollow veins of rabbits exhibit a rather high degree of thromboplastic, anticoagulant and fibrin-stabilizing activity. There is little fibrinolytic activity of the tissues in these animals.

2. Hypodynamia increases the thromboplastic properties of the inner and middle layers of the aorta.

3. The fibrin-stabilizing activity of all tissues increases.

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